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Efficacy and Safety of B/F/TAF in Treatment-Naïve People With HIV Aged ≥ 50 Years: 5-Year Follow-Up From Two Phase 3 Studies

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Conclusions

- Over 5 years of follow-up, B/F/TAF maintained high rates of virologic suppression in treatment-naïve people with HIV aged ≥ 50 years, including those with suboptimal adherence
  - Virologic suppression (HIV-1 RNA < 50 c/mL) rates were high and similar between participants aged ≥ 50 and < 50 years
  - The proportion of participants with adherence ≥ 85% was high in both groups; however, participants aged ≥ 50 years were more likely to have adherence ≥ 95% in comparison with those aged < 50 years
- No treatment-emergent drug resistance was reported
- B/F/TAF well tolerated and resulted in no clinically significant changes from baseline in bone, renal, and metabolic parameters that were similar between age groups
- Study drug discontinuations due to AEs were low in both age groups
- These data support B/F/TAF use for long-term management of HIV in older people with HIV who have no prior HIV treatment experience

Plain Language Summary

- The number of people with human immunodeficiency virus type 1 (HIV-1) aged 50 years or older is increasing
- B/F/TAF is a single pill used to treat HIV-1 in many countries
  - The pill combines three medications: bictegravir (B), emtricitabine (F), and tenofovir alafenamide (TAF)
  - International guidelines recommend using B/F/TAF:
    - For people with HIV-1 starting their first treatment
    - For people who have undetectable levels of HIV-1 in their blood after taking other treatments
- This study looked at data from two clinical studies of B/F/TAF to find out if it was effective and safe for people with HIV-1 aged 50 years or older
- After 5 years of treatment, B/F/TAF was very effective at lowering the amount of HIV-1 in the blood of people aged 50 years or older and those who were younger
- Side effects were rare and were similar in people from both age groups
- This study shows that B/F/TAF is an effective long-term treatment for older people with HIV-1

Introduction

- An increasing proportion of people with HIV are aged ≥ 50 years, with a greater burden of age-related comorbidities[1,2]
- Adverse drug events from antiretroviral therapy (ART) and concomitant drugs may occur more frequently in older persons with HIV than in younger people with HIV[2]
  - Bone, kidney, metabolic, and cardiovascular health of older individuals with HIV may be particularly affected[2]
- Therefore, optimizing HIV treatment in older people is important
  - Long-term analyses of ART in this population are limited
- Bictegravir, emtricitabine, and tenofovir alafenamide (B/F/TAF) demonstrated efficacy and safety through 5 years in the Phase 3 studies 1489 (NCT02607930) and 1490 (NCT02607956) in people with HIV who are treatment naïve[3-5]
  - However, outcomes with B/F/TAF in older people with HIV have not been reported in these studies

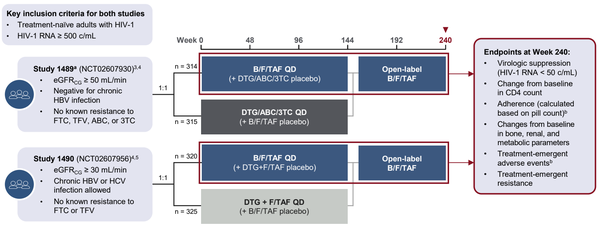
Objective

- To assess the efficacy and safety outcomes with B/F/TAF through 5 years (Week 240) of first-line therapy in treatment-naïve people with HIV aged 50 years and older in two Phase 3 studies

Methods

Study Design

- Post hoc pooled analysis of participants who received B/F/TAF in the 144-week randomized phase, and the 96-week open-label extension, of two randomized, double-blind, multicenter, Phase 3 studies



[a]Participants were also required to be HLA-B*5701 negative for inclusion in the study.
[b]Through the end of the study.
3TC, lamivudine; ABC, abacavir; B, bictegravir; c, copies; CD4, cluster of differentiation 4; DTG, dolutegravir; eGFRCG, estimated glomerular filtration rate by Cockcroft-Gault equation; F/FTC, emtricitabine; HBV, hepatitis B virus; HCV, hepatitis C virus; HLA, human leukocyte antigen; QD, once daily; TAF, tenofovir alafenamide; TFV, tenofovir.

Results

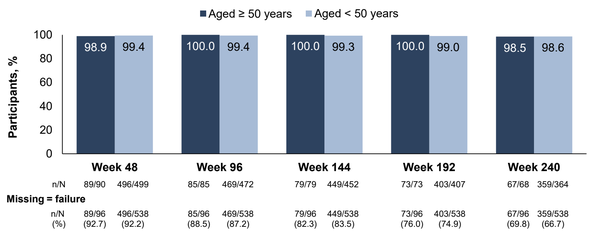
Baseline Demographics and Clinical Characteristics

		Aged ≥ 50 Years n = 96	Aged < 50 Years n = 538
Age, years, median (Q1, Q3)		55 (52, 60)	30 (25, 37)
Male sex at birth, n (%)		81 (84)	484 (90)
Region, n (%)	US	56 (58)	365 (68)
	Ex-US	40 (42)	173 (32)
Race, n (%)	White	59 (62)	304 (57)
	Black	30 (32)	181 (34)
	Other[a]	6 (6)[b]	52 (10)[b]
Hispanic or Latine ethnicity, n (%)		11 (11)	144 (27)[c]
HIV-1 RNA, log_{10} c/mL, median, (Q1, Q3)		4.48 (4.00, 4.93)	4.41 (4.00, 4.86)
HIV-1 RNA > 100,000 c/mL, n (%)		23 (24)	96 (18)
CD4 cell count, cells/μL, median (Q1, Q3)		436 (235, 601)	442 (299, 590)
Medical history, n (%)	Diabetes mellitus	16 (17)	22 (4)
	Hyperlipidemia	39 (41)	48 (9)
	Hypertension	46 (48)	52 (10)

[a]Includes American Indian or Alaska Native, Asian, Native Hawaiian or Pacific Islander, and other. [b]Race data not available for one participant. [c]Ethnicity data not available for two participants.
c, copies; CD4, cluster of differentiation 4; Q, quartile.

- As expected, comorbidities such as diabetes, hyperlipidemia, and hypertension were more frequent among participants aged ≥ 50 years

HIV-1 RNA < 50 copies/mL (Missing = Excluded) Through Week 240



- Rates of virologic suppression with B/F/TAF were high through Week 240 in both age groups

Resistance Analysis Through Week 240

- No treatment-emergent resistance to the components of B/F/TAF was reported in any participant in either group through Week 240

Immunologic Outcomes at Week 240

- At Week 240, CD4 cell count increased from baseline among both participants aged ≥ 50 and < 50 years (mean [SD] change from baseline: +291 [221] and +347 [238] cells/μL, respectively; the increase was similar between groups; $P = 0.07$[a])

[a]*P* value for ≥ 50 and < 50 years group comparison from an analysis-of-covariance model, adjusted by the baseline HIV-1 RNA (≤ 100,000 vs > 100,000 copies [c]/mL) and region stratum.

Adherence by Pill Count Through Week 240

	Aged ≥ 50 Years n = 96	Aged < 50 Years n = 538
Participants who returned ≥ 1 bottle, n (%)	93 (97)	531 (99)
Adherence rate through Week 240[a]		
Median (Q1, Q3), %	98 (97, 99)	97 (93, 99)
≥ 95%, n (%)	77 (83)	352 (66)
≥ 85% to < 95%, n (%)	11 (12)	140 (26)
< 85%, n (%)	5 (5)	39 (7)

Adherence was calculated based on pill count for B/F/TAF only. The denominator for percentage of drug adherence category was the number of participants who returned ≥ 1 bottle and had calculable drug adherence.
[a]Through the end of the study.
B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; Q, quartile.

- The median B/F/TAF adherence rate was high among both groups
  - 95% of participants aged ≥ 50 years and 93% of those aged < 50 years had ≥ 85% adherence
- A greater proportion of participants aged ≥ 50 versus < 50 years had ≥ 95% adherence (83% vs 66%; $P = 0.0015$; Fisher exact test)
- In participants with < 85% adherence, 100% (3/3 of those aged ≥ 50 years and 16/16 of those aged < 50 years) had HIV-1 RNA < 50 c/mL on B/F/TAF at Week 240 by missing = excluded (M = E) method[a]

[a]M = E analysis of all data collected up to 1 day after permanent discontinuation of study drug.

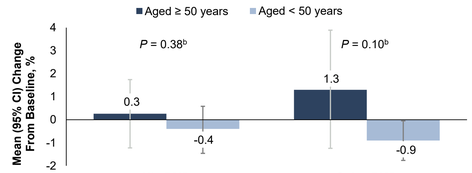
TEAEs Through Week 240[a]

	Aged ≥ 50 Years n = 96	Aged < 50 Years n = 538
Any TEAE	90 (94)	514 (96)
Study drug–related TEAEs	25 (26)	153 (28)
Any Grade 3 or 4 TEAEs	30 (31)	102 (19)
Study drug–related Grade 3 or 4 TEAEs	4 (4)[b]	5 (< 1)[c]
Any serious TEAEs	33 (34)	103 (19)
Study drug–related serious TEAEs	2 (2)[d]	3 (< 1)[e]
Study drug discontinuation due to TEAE	4 (4)[f]	6 (1)[g]
Death	6 (6)[h]	2 (< 1)[i]

Data shown as n (%). N values represent numbers of participants.
[a]Through the end of the study. [b]Atrial flutter, dizziness, and acute pancreatitis (in the same participant); abdominal pain, atypical chest pain, and elevated liver enzyme levels (n = 1 each). [c]Abdominal distention, diarrhea, generalized tonic-clonic seizure, osteoporosis, and suicide attempt (n = 1 each). [d]Atrial flutter, acute pancreatitis, and dizziness (in the same participant); and chest pain (n = 1 each). [e]Generalized tonic-clonic seizure, spontaneous abortion, and suicide attempt (n = 1 each). [f]Cardiac arrest, chest pain, COVID-19, and obesity (n = 1 each). [g]Abdominal distension, dyspepsia, toxicity due to various agents, intervertebral discitis, and tension headache (n = 1 each). [h]Cardiac arrest (n = 2); hypertensive heart disease with congestive heart failure, poorly differentiated gastric adenocarcinoma, COVID-19, and drug toxicity (n = 1 each). [i]Hemorrhagic hypovolemia (self-inflicted), and an unknown cause (n = 1 each).
TEAE, treatment-emergent adverse event.

- Study drug–related treatment-emergent adverse events (TEAEs) experienced by ≥ 5% of participants in the ≥ 50- or < 50-year-old group, respectively, were nausea (5% and 4%), headache (4% and 5%), and diarrhea (4% and 5%)
- Rates of study drug discontinuations due to TEAEs were low in both groups
- Grade 3 or 4 TEAEs, serious TEAEs, and study drug discontinuations due to TEAEs were more frequent in participants aged ≥ 50 years than in those aged < 50 years, as expected in an older population

Change From Baseline in Bone Mineral Density (BMD) at Week 240[a]



	Hip BMD		Spine BMD	
	Aged ≥ 50 years	Aged < 50 years	Aged ≥ 50 years	Aged < 50 years
n at baseline	21	126	21	130
n at Week 240	21	126	21	130
BMD at baseline, g/m², mean (95% CI)	1.0 (0.94-1.07)	1.1 (1.03-1.08)	1.1 (1.06-1.21)	1.2 (1.13-1.19)

Baseline value was defined as the last non-missing value obtained on or prior to the first dose of B/F/TAF.
[a]BMD values were from study 1489 only. [b]*P* values were from an analysis-of-variance model including age group as a fixed effect.
B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; BMD, bone mineral density.

- Changes from baseline to Week 240 in hip and spine bone mineral density were minimal and similar between groups

Change From Baseline in Renal and Metabolic Parameters at Week 240

		Aged ≥ 50 Years n = 96	Aged < 50 Years n = 538		*P* Value
		Median (Q1, Q3)	n	Median (Q1, Q3)	n	
eGFR,[a] mL/min	Baseline	99.2 (83.6, 114.0)	96	126.3 (108.5, 146.8)	538	< 0.0001
	Change at Week 240	-10.5 (-19.6, 2.4)	67	-7.7 (-19.4, 3.0)	363	0.30
Body weight, kg	Baseline	79.3 (70.7, 89.9)	96	75.9 (67.3, 87.1)	538	0.0285
	Change at Week 240	4.8 (0.7, 10.2)	68	6.4 (2.4, 12.0)	363	0.09
TC:HDL ratio[b]	Baseline	4.1 (3.2, 5.0)	93	3.7 (3.0, 4.5)	526	0.0017
	Change at Week 240	-0.3 (-0.9, 0.4)	65	0.1 (-0.4, 0.6)	345	0.0044

For more information on metabolic and renal outcomes, please scan the QR code

Baseline value was defined as the last non-missing value obtained on or prior to the first dose of B/F/TAF. *P* values were from the 2-sided Wilcoxon rank sum test.
[a]By Cockcroft-Gault equation. [b]Only laboratory measurements under fasting status are summarized.
B/F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; Q, quartile; TC, total cholesterol.

- At Week 240, changes in estimated glomerular filtration rate were not clinically significant and were similar between groups
- Despite significant differences between groups at baseline, changes in metabolic parameters at Week 240 were not clinically significant, except for changes in body weight in those who were underweight or had cachexia at baseline

Treatment-Emergent Diabetes and Hypertension Through Week 240

	Aged ≥ 50 Years n = 96		Aged < 50 Years n = 538		*P* Value
	n (%)	Participants With Available Data, n	n (%)	Participants With Available Data, n	
Treatment-emergent diabetes[a]	4 (5)	78	9 (2)	515	0.0782
Treatment-emergent hypertension[a]	10 (20)	51	61 (12)	489	0.1877

[a]Participants with a medical history of diabetes/hypertension were excluded. *P* values were from the Fisher exact test.

- Proportions of treatment-emergent diabetes and hypertension were numerically higher among participants aged ≥ 50 versus < 50 years

Lipid-Modifying Agent Use Through Week 240

	Aged ≥ 50 Years n = 96	Aged < 50 Years n = 538	*P* Value
At baseline, n (%)	21 (22)	11 (2)	< 0.0001
Initiation during the study, n (%)	20 (21)	27 (5)	< 0.0001

P values were from the Fisher exact test.

- Proportions of participants using lipid-modifying agents at baseline and initiating them during the study were higher among those aged ≥ 50 versus < 50 years

References: **1.** HIV.gov. https://www.hiv.gov/hiv-basics/living-well-with-hiv/taking-care-of-yourself/aging-with-hiv (accessed August 1, 2024). **2.** DHHS. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-arv/guidelines-adult-adolescent-arv.pdf (accessed August 1, 2024). **3.** Gallant J, et al. *Lancet*. 2017;390:2063-72. **4.** Sax P, et al. *EClinicalMedicine*. 2023;59:101991. **5.** Sax P, et al. *Lancet*. 2017;390:2073-82.

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